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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,491	05/31/2001	David H. Raulet	B01-088-1	8724

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 10/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/871,491	RAULET ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Claims 39-54 have been added.

Claims 19-38 have been cancelled.

Claims 39-54 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

3. Claims 39-44 and 51-54 are objected to because of the following informalities: the dependent claims 40-44 and 52-54 do not further limit from the independent claims, 39 and 51 and are deemed duplicate claims. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 39-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting prostate tumor growth and primary mammary tumor growth in a mammalian host, does not reasonably provide enablement for the said method including the administration of a NKG2D transduced

cell to a mammalian host *predisposed* to having the said tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As set forth in Paper number 6, mailed March 25, 2003 Applicants have set forth evidence that the TRAMP-derived murine prostate cancer cell line, TRAMP-C2 (C2) have been transduced with NKG2D-ligands and administered to C57BL/6 male mice. The results provided in the bridging paragraphs of pages 20, 21 and 22, 23 support *in vivo* administration of NKG2D-ligand transduced cells can elicit an antitumoral response and reduce tumor incidence and severity of prostate lesions. The methodology listed in the specification is not commensurate in scope with claims, particularly the method of inhibiting tumor growth in a host predisposed to having a tumor.

There is no guidance in the specification as to how to determine and select a population of individuals, which may of may not eventually have cancer. Preventing a disease is just as complex a process. It is not clear what parameters would one skilled in the art use in order to identify a population of subjects that cancer could be prevented. It is also not clear what symptoms one of skill in the art would need to identify before possibly treating a patient. While it is art known that clinicians are capable of implementing both screening and surveillance and the type of screening test used and the intervals at which it is performed are based on risk stratification, which also serves as the basis for selecting potential candidates for possible prevention. However, like most screening procedures determining whether a population will eventually be struck with a disease is not full proof.

There would also need to be some valid amount of direction or guidance, as well as presence or absence of working examples presented in the specification that would enable one skilled in the art to perform the method as presented in the recited claims. It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte Forman, 230 USPQ 546 BPAI, 1986.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 39-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 39, 40, 51 and 52 are vague and indefinite in the recitation "determined to have ...tumor". Independent claims 39 and 51 have already set forth that the host has a tumor, hence there is no need to reiterate so in dependent claims 40 and 52, respectively.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 39-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diefenbach et al. (Nature Immunology 1(2): 119-126, 2000), and further in view of WO 98/19167 (7 May 1998). Diefenbach teaches a method of transient transfection of NKG2D-binding moieties, Raeβ1 and H-60 ligands to COS-7 cells, see Figure 3b caption, as well as bridging paragraph of columns 1 and 2 on page 121. Diefenbach also teaches detection of resultant inhibition of tumor growth via assays determining cell killing and interferon (IFN)-γ production by natural killer (NK) cells. Diefenbach does not teach the methods for inhibiting prostate tumor growth or primary mammary tumor growth in a mammalian host comprising administering to the said host a composition comprising a multivalent NKG2D-binding moieties (i.e. MICA, MICB and ULBP) effective to inhibit growth of the tumor and detection of the resulting inhibition of tumor growth.

WO 98/19167 teaches a method for enriching or expanding a cell population and increasing the expression of MHC-related molecules such as NKG2D ligands, MICA or MICB in a human cell by providing the said ligand polypeptides to the human cells for the treatment of certain disease states such as cancer, see Abstract; page 5, lines 22-25; and page 6, lines 4-12. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to transduce other NKG2D binding moieties such as MICA, MICB or ULBP to a host-compatible cell in order to inhibit prostate tumor growth, as well as primary mammary tumor growth. Inevitably one of ordinary skill in the art at the time the claimed invention would have detected the resulting inhibition of tumor growth. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of (1)

Diefenbach on expression of NKG2D ligands by target cells triggers NK cell cytotoxicity and IFN-γ secretion by NK cells through ligand interaction with NKG2D, which stimulates host immunity, see abstract; and (2) WO 98/19167 on the use of MHC-related molecules can be expressed to enhancing the immune response and aid in the treatment of cancer.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
27 October 2003